EDITORIAL ARTICLES.

PORTER ON THE INDICATIONS TO BE DRAWN FROM THE URINE AS TO THE SAFETY OF ANÆSTHETICS.[1]

AT a meeting of the Clinical Society of the New York Post-Graduate Medical School, Dr. William H. Porter presented a paper upon this subject which contains some original and well-supported views as to the action of anæsthetics, and the indications as to their safety presented by the state of the urinary excretion.

After describing the characteristics of normal urine and the transmutation changes which regularly occur in it when exposed to the air, which are indicative of a normal state of the system, and one in which the nutritive vitality is well maintained, he states that patients presenting such a normal urinary excretion bear etherization and chloroformation without ill effects as a general rule. When, however, the quantity of urine being normal, or below the standard amount, the color is pale and the density low, it indicates that digestion and absorption are imperfectly effected, and that nutrition is below the normal standard, and vital activity deteriorated. Patients in such instances, while they do not necessarily succumb to the damaging effects of anæsthetics, may not bear the etherization or chloroformation well, and often require stimulation before the administration and during the anæsthetic period. Chloroform in these cases is equally as safe as ether.

If the urine is scanty, high-colored and of high density, it is usually associated with a deficiency of urea and an excess of uric acid, and often contains a number of other by-products, all of which are due to the incomplete oxidation of the proteid molecule. The urine may be normal in amount, of normal or higher color, yet the density be abnormally high, but with a diminished amount of urea.

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The urine may also be abundant in quantity, light in color, deficient in urea, and still of high density. This is usually due to the presence of glucose with its molecular weight of 180. All these conditions are clearly explained by a study of the true chemical composition of the urine and the molecular structure of the urea, uric acid and the other by-products of proteid tissue waste.

When the normal or highest oxidation of the proteid molecule is maintained the most perfect end-product is urea, a nitrogenous body of great solubility and low molecular weight. Therefore normal urine has the density already described, and readily undergoes the transmutation changes which speedily result in the formation of the ammonio-magnesium phosphate crystals in abundance.

He believes that the scanty flow of urine, of high color and density, and a deficient production of urea, is due to incomplete oxidation of the proteid molecule with the formation of uric acid, lactates, oxalates, etc., all of which have a higher molecular weight than urea. For instance, the molecular weight of urea is 60, that of uric acid is 168, and its urates 190. In other words, each molecule of uric acid is 2.6 times heavier than urea; and the urates, 3.16 times heavier. This, however, is not so bad as are some of the other conditions, as the uric acid molecule carries out of the system twice as much nitrogen as urea. But when the uric acid is present in abundance at the expense of the urea, it indicates incomplete oxidation and impaired nutrition, with some granular change in the liver, kidneys and glandular organs. Such cases bear anæsthetics poorly and often succumb a few days later.

If to the urine containing uric acid there is added the oxalates which have a molecular weight of 129, and the lactates with their molecular weight of 112, the density of the urine will be still higher. These by-products indicate a still lower state of oxidation and a greater loss of inherent vitality. When this is the case the probabilities regarding anæsthesia are still more uncertain.

He calls attention to still another variety of scanty urine of high density which is indicative of the lowest grade of nutritive vitality, and in which all the glandular organs are very much impaired, and yet albumen casts and glucose may not appear in the urine. It is that variety in which the nitrogenous waste that should pass out of the body through the biliary secretion as bile salts and coloring matters pass out through the renal organs. When this is the case the urine, unless very abundant in quantity, is very dark in color, the density from 1030 to 1040; and it may rise as high as 1060. The high density in these cases is explained by the great molecular weight of the bile salts and coloring matter as compared with urea. The glycocholate of soda, for instance, carrying only one atom of nitrogen, or one less than urea, has a molecular weight of 487, and, therefore, is 8.11 times heavier than urea. The taurocholate of soda, also containing only one nitrogen atom to the two in urea, has a molecular weight of 537, and is, therefore, 8.95 times heavier than urea.

The bile coloring matters also have a high molecular weight. That of bilirubin being 286 and the biliverdin 322, the former is, therefore, 4.76 while the latter is 5.39 times heavier than urea. Urine of this composition indicates a very great disturbance in the assimilative powers of the system, and indicates a general retrograde change in all the glandular organs and tissues of the body.

It is the opinion of the author that etherization and chloroformation followed by operative interference in cases of this kind are very apt to terminate fatally. Absence of albuminous casts and glucose have led to the supposition that the patient was in a good condition for etherization. He has made the necropsy in a number of fatal cases of this nature, in which the action of the ether was just sufficient to cause a rapid dissolution of the glandular organs, toxic symptoms and speedy death.

A study of this class of cases has led him to believe that when the urine contains an abundance of these by-products of proteid oxidation with a high specific gravity and no albumen casts or glucose, the patient is still in a very precarious condition, and often more likely to succumb under the anæsthetic than when that state of sub-oxidation exists which produces albumen and glucose. Of course, when casts are present it indicates a more marked retrograde change in the kidneys, and chloroform, he thinks, is to be preferred to ether. According to Dr. Porter, these unobserved glandular changes cause most of the fatal results in surgery. Were it not for these weak points in the system, almost every operative case ought to recover, inasmuch as the mechanical part of surgery has been brought by antiseptics almost to absolute perfection.

The author then goes on as follows, to show how the anæsthetic is a factor in producing these bad results, and gives a very clear statement of the physiology of ether and chloroform anæsthesia.

Ether is an hydro-carbon, *hydroxyl* derivative, being composed of carbon, hydrogen and oxygen ($C_4 H_{10} O$); while chloroform is an hydro-carbon, *chlorine* derivative, being composed of carbon, hydrogen and chlorine ($C H Cl_3$).

In using either ether or chloroform, anæsthesia cannot be produced so long as the requisite amount of oxygen is supplied to the system.

The activity of the medullary centres is dependent upon the active supply of fully oxygenated blood. Therefore it is but just to assume that the chief factor in producing the anæsthetic state, both with the ether and the chloroform, is the direct result of the displacement or shutting out of the oxygen supply from the respiratory passages, and thus from the blood, by the anæsthetic used. This is unquestionably true with the nitrous oxide ($N_2 O$), also with ether and chloroform.

This taking away from the system of the great heat-producing element, which is indisputably the prime agent in stimulating the whole animal chemistry into action and maintaining its normal activity, is the chief function of the anæsthetic. At the same time there is rapidly induced an imperfectly oxygenated state of the blood, so that the natural stimulation of oxygenated blood upon the cardiac, respiratory and vasomotor centres is reduced to a minimum point compatible with a continuance of the cardiac and respiratory actions.

When the natural peripheral irritation of the centripetal nerves by the heat produced through the oxidation of the food products is suspended or totally abolished, and the oxygen in the blood has been reduced until only the cardiac and respiratory centres are capable of being irritated sufficiently to keep only the heart and respiration in motion by this low percentage of oxygen in the blood, the patient is thrown into a quiescent and dead state, commonly called anæsthesia.

From this condition the patient cannot be aroused except by restoring the oxygen supply, re-establishing the peripheral heat production, and raising the percentage of oxygen in the blood to the normal standard until it will normally excite the central cells into greater activity. In some instances, when the anæsthesia is prolonged or pushed too strongly, the sub-oxidation of the body is carried to such a profound degree that oxidation cannot be re-established by natural means. When this is the case, extraneous heat has to be applied to excite the reflex activity of the nervous mechanism until oxidation and natural heat-production can be re-established to keep up the nerve action.

The author, following this line of argument a step further, says that only one conclusion can be drawn, namely, that the administration of ether, for the purpose of producing anæsthesia, immediately develops within the system a state of general sub-oxidation directly in proportion to the amount of oxygen that is shut out of the air passages.

This absence of oxygen in the blood induces general mal-nutrition by arresting oxidation of the proteid fat and glucose molecules of the food-stuffs. As a secondary result, the products of tissue-waste are at first decreased, then incompletely formed and, in many instances, are irritating or poisonous in character. After the anæsthesia they are abundant and incompletely formed.

He claims from these facts that it becomes apparent at once that the system is chemically damaged by ether anæsthesia, mal-nutrition induced, extra strain imposed upon the physiological mechanism, and all the glandular organs called upon to perform extra work upon a defective nutritive supply. When this stage is reached all the functions are abolished except the cardiac and respiratory. In a perfectly normal individual this extra strain can be borne almost with impunity for hours.

When the physiological economy is below par, the reverse often holds true, and alarming and fatal consequences are witnessed. In this latter case there is often developed immediately, or within a few hours after the anæsthesia, symptoms which are called "septic," and are followed by death.

Since the introduction of antiseptics, and by careful post-mortem observation, it has been found that these so-called septic symptoms are developed without any septic infection through or from the wound.

He believes that they are the results of the damaging effects upon the system resulting from the sub-oxidation induced by the anæsthetic which has shut out the oxygen and arrested glandular action. This results in rapid retrograde changes in the epithelial cells of the glands, with a retention of the excretory products within the system, which should now, more than ever, be eliminated.

Thus ether causes the death of a large number of cases, but in a day or two after the anæsthesia, rather than upon the operating table.

In those cases in which there exist in the urine these positive evidences of retrograde changes in the glandular organs of the body and a state of universal sub-oxidation, there is reason to suspect unpleasant symptoms, or even death during anæsthesia. But in most instances death is delayed until a few hours or a day or two after the operation; and the fatal results are brought about by the excretory organs in their previously damaged condition being unable to cope with a further state of sub-oxidation, and the augmented demand upon their fundamental activity. At this stage albumen and casts usually appear when not present before.

He very aptly observes that this delay in the fatal result takes the odium off the ether as compared with chloroform, while the ether still remains equally responsible, and probably causes as many if not more deaths than chloroform.

Owing to the great volatility of ether, the heat of the body rapidly drives it from the air passages, so that it requires a considerable volume and some time to displace the air from the lungs and cause the sub-oxidation, arrest of functions, and, finally, the condition called anæsthesia.

He gives still another reason why ether is slow in producing anæsthesia, namely, that it is a readily inflammable compound, and to a certain extent is oxidized in the epithelial structures of the respiratory passages, with the production of carbon di-oxide and water, and a definite yield of heat for each gramme oxidized. Each gramme of ether consumed in this way requires for its complete oxidation 2.59 grammes of oxygen, or about the same as is required in the consumption of fat and alcohol.

This rapid oxidation of the ether also aids in shutting out the oxygen from the blood. But at the same time it generates considerable heat in the lungs, which irritates the peripheral ends of the centripetal nerves of the respiratory system. This explains why the respiration and circulation are well sustained during the primary stage of ether anæsthesia, and shows why the heart and lungs are not apt to fail early, as occasionally occurs with chloroform.

It also illustrates the apparent failure of the respiratory act as the anæsthesia deepens. The reflex action of the respiratory nerves is exhausted by this rapid and continuous production of heat, and at this stage the reflex respiratory irritation ceases to be a factor in keeping in motion the medullary centres. The respiratory centre has not yet accustomed itself to the method of irritation through the blood only. Now the deep pressure in the epigastric region, or the quick and forcible compression of the chest is just enough to keep the medullary centres active until they accustom themselves to the poorly oxygenated blood supply to keep up their motion.

By the aid of these physiological phenomena, it is clear that the heart and circulation must fail first in the poisoning effects of ether anæsthesia. The medullary centres are primarily kept in motion by oxygenated blood and are only secondarily influenced by reflex impulses; therefore, so long as blood containing the requisite amount of oxygen continues to reach the medulla its functional activity must continue.

The ether, mechanically, and by its oxidation in the air passages, deprives the blood of its requisite supply of oxygen, therefore, failure of the circulation in the medulla is the first chain in the depressing influences of ether anæsthesia.

Owing to the lack of the peripheral reflex stimulation and the previously overworked condition of the centripetal pulmonary nerves, as explained by the exhalation of the ether in the lungs, the respiratory centre is apt to be somewhat depressed as compared with the cardiac, so that when the two are compelled to depend exclusively upon the irritation of the imperfectly oxygenated blood flowing through the medulla for their activity, the respiratory centre usually fails to respond, while the cardiac centre continues to innervate the heart. If for any reason there is a previous exhaustion of the cardiac centre, it shows evidence of primary failure. Thus elucidating the contradictory evidence of the Hyderabad Commission.

He then takes up the subject of chloroform, which acts upon the same principle as nitrous oxide and ether by shutting out the air from the respiratory passages, and the oxygen from the blood.

Chloroform is a heavy liquid having a molecular weight of 119.4 to that of 74 for ether. It is easily and rapidly drawn into the air passages, and not being very volatile is not readily displaced, so that very much less chloroform is required to displace the air and shut the oxygen out of the blood than holds true when using ether.

The persistent retention of chloroform in the cavity of the respiratory chambers explains why a very little can be given at a time, and shows how a little crowding of the chloroform easily asphyxiates the patient and causes failure both of the heart and lungs. As the chloroform cannot be oxidized and made to yield heat like the ether, the failure of the heat and respiration comes suddenly. Before there is time to excite the respiratory and cardiac centres by extraneously applied heat, and re-establish the natural heat products by normal body oxidation, the centres have ceased to act forever.

He is of the opinion that intelligently and carefully administered this accident cannot occur, and the use of chloroform is just as safe as that of ether.

With chloroform this deprivation of the system of its oxygen can be accomplished without any expenditure of oxygen as occurs with ether, and consequently no extra heat is produced which irritates the system and aids in intensifying the sub-oxidation; in other words, properly handled, chloroform produces complete sub-oxidation quickly and with the least possible shutting out of the oxygen from the blood. Therefore, scientifically used in perfectly normal individuals, chloroform is less damaging to the animal economy, and much safer than ether. And, in fact, he claims that in perfectly normal individuals, if properly administered, ether and chloroform, while damaging the true physiological economy in producing anæsthesia, can yet be given with absolute safety.

Anæsthetics, however, are rarely administered to normal individuals; they are always more or less unsound, otherwise there would be no occasion to use these agents. Therefore an entirely different problem confronts us, and necessitates a thorough understanding of the physiological economy, and how to find it out through the urine.

After this thorough discussion of the action of the anæsthetics, Dr. Porter goes on to explain their bad effects as follows:

Ether, if given too quickly and too freely, may cut off the oxygen so completely as to cause instant death; this rarely happens. In other more or less pathological subjects, the rapid oxidation of the ether in the lungs wears out the irritability of the centripetal respiratory nerves in the lungs. The blood-vessels rapidly expand, which, together with a large production of water from the oxidation of the ether, induces a fatal œdema of the lungs.

Usually in the early stages of anæsthesia, the pulmonary blood-vessels contract, but as the anæsthesia deepens they relax and with the water generated from the oxidation of the ether there is always a free flow of bronchial mucus, but not to a sufficient degree to produce any alarming symptoms.

Occasionally a rapid oxidation of a large quantity of the ether exhausts the oxygen supply, and, by over stimulating the centripetal nerves, and through these the central ganglion cells, causes a rapid exhaustion of the nervous system, followed by a sudden respiratory and cardiac failure and death.

Thus we have an explanation for the possible development of sudden death by ether anæsthesia.

He is, however, inclined to believe that more frequently death due to ether anæsthesia comes on after the administration, and is caused by the secondary glandular degeneration and consequent toxæmia induced therefrom.

Though chloroform has been found to be perfectly safe as a rule where properly administered, still there are a few cases that succumb suddenly when attempting to take chloroform and apparently without any satisfactory reason. Dr. Porter assumes that this never occurs in perfect states of health, but only in those that are more or less pathological.

He advances the hypothesis that these sudden deaths are due to an oxidation of the proteid molecule in the epithelial cells of the respiratory passages, which results in the formation of free ammonia ($N\ H\ 3$). This unsatisfied radical in the presence of the heat of the respiratory chambers and the free oxygen, results in the decomposition of the chloroform in one of three methods; all of which give rise to the formation of suffocating and poisonous gases; which fill the deeper air passages and suddenly and completely shut out the oxygen from the blood. Thus arresting life at once.

These chemical changes he gives as follows: $C\ H\ Cl_3$ plus $N\ H_3$ plus $O = C\ O\ Cl_2$ plus $N\ H_4$ plus Cl, or $C\ H\ Cl_3$ plus $N\ H_3$ plus $O = C\ O\ Cl_2$ plus $N\ H_4\ Cl$, or $2(C\ H\ Cl_3)$ plus $2(N\ H_3)$ plus $2(O) = C\ Cl_4$ plus $2(N\ H_4\ Cl)$ plus $C\ O_2$.

The following practical deductions are drawn from this chemico-physiological analysis of chemical phenomena:

(1) That ether and chloroform act upon the same principles, but with results developed by slightly different methods.

(2) That both are capable of producing death at the time of the anæsthesia; chloroform more frequently than ether.

(3) That ether causes as many, if not more, deaths than chloroform, but the fatal issue is delayed until the patient has been removed from the operating table.

(4) That by a careful study of the density of the urine and its causes, we are in possession of exact information by which we can determine the precise nutritive condition of the system, and be forewarned as to the possible outcome of the anæsthesia. It also enables us to judge which anæsthetic is best adapted to the individual case in question.

(5) We are taught that neither ether nor chloroform should be administered until the glandular organs, in their necessarily damaged states, are put in the best possible condition to endure this extra strain. When this is a general rule many cases that now prove fatal will be saved.

(6) It teaches that every public institution should have a paid physician who is competent to examine the urine, and determine through it the status of the physiological economy before giving the anæsthetic. It should also be the duty of this same physician to administer the anæsthetic, for he alone knows best which anæsthetic to select with a given condition of the system, and is also better able to guide the patient safely through the anæsthesia than one who knows nothing of the constitution of the patient except from a second party.

(7) While it is clear that death in some instances is directly due to the primary effects of the ether and chloroform, and in others to secondary effects, it should not deter us from using them, but stimulate us to be more thorough masters of their actions upon the system, and thus to guard against their ill effects. When all this is accomplished, chloroform will probably hold the first place as an anæsthetic.